

Notice of Allowability

Application No.

09/554,980

Applicant(s)

KOLESNICK ET AL.

Examiner

Fozia M Hamud

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included
rewritten (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS
NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative
of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

☒ This communication is responsive to 12/29/03.

☒ The allowed claim(s) is/are 1, 2, 3, 4, 6 and 7 (now renumbered 1-6, respectively).

☒ The drawings filed on 19 May 2000 are accepted by the Examiner.

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the
International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements
noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF
INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

(a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached

1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.

(b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of
Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of
each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the
attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

☐ Notice of References Cited (PTO-892)

☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____

☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material

5. ☐ Notice of Informal Patent Application (PTO-152)

6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____

7. ☒ Examiner's Amendment/Comment

8. ☒ Examiner's Statement of Reasons for Allowance

9. ☐ Other _____

Examiner's Amendment

1. An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

Authorization for this Examiner's Amendment was given in a telephone interview with Attorney Benjamin A. Adler, on 26 March 2004.

2. The application has been amended as follows:

IN THE CLAIMS:

In claim 1, line 2, after "animal" insert ---, said method---

In claim 1, line 6, after "animal" delete "; and inhibiting" substitute therefor --- to inhibit---

In claim 1, line 8, after "sphingomyelin" insert ---, ---

In claim 4, line 3, after "animal" insert ---, said method---

In claim 4, line 7, after "animal" delete "; and inhibiting" substitute therefor --- to inhibit---

In claim 4, line 9, after "sphingomyelin" insert ---, ---

REASONS FOR ALLOWANCE:

3a. Instant claims are drawn to a method of treating endotoxic shock or a method of inhibiting lipopolysaccharide-induced endothelial apoptosis, by administering basic fibroblast growth factor (b-FGF) to an animal. The rejection of instant claims 1, 2, 4, 6, 10, made under 35 U.S.C. 102(e) as being anticipated by Jain et al. (U. S. Patent 6,010,712), is withdrawn, because Applicants' argument that endotoxic shock is not sepsis is persuasive.

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Applicants submit a recent article by Reidemann et al. (The Enigma of Sepsis, Journal of Clinical Investigation, Volume 112 (4): 460-467 (2003)) that discusses the clinical definition of sepsis and treatments thereof over the last 40 years. Reidemann et al. disclose that currently there is a general agreement among researchers in the field that lipopolysaccharide injection may serve as a model for endotoxic shock but not for sepsis, (see page 462, column 2). Reidemann et al. also disclose that at present it is believed that Gram-positive bacteria are predominantly the microorganisms responsible for sepsis, whereas in the late 1970s and 1980s it was held that predominantly Gram-negative bacteria were predominantly the microorganisms responsible for sepsis, (see page 460, first paragraph). Accordingly, a person having ordinary skill in this art could reasonably conclude that endotoxic shock and sepsis are two distinct pathophysiological states.

Instant specification discloses that lipopolysaccharide induces ceramide generation from sphingomyelin, which subsequently induces apoptosis in the endothelial microvasculature, resulting in endotoxic shock. Instant specification also shows that b-FGF abrogated lipopolysaccharide-induced apoptosis in the endothelium of the intestine and lung of C57BL/6 mice, (see page 25 and Figure 6A).

Therefore, the method of treating sepsis by administering b-FGF to an animal suffering from said condition, taught by Jain et al is patentably distinct from the instantly claimed method of treating endotoxic shock, or the method of inhibiting lipopolysaccharide-induced endothelial apoptosis, by administering basic fibroblast growth factor to an animal.

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3b. Also the rejection of claims 1, 3, 4 and 7 under U.S.C. § 103 as being unpatentable over Jain et al is withdrawn, because the Jain et al reference neither teaches nor suggests the method of treating endotoxic shock or the method of inhibiting lipopolysaccharide-induced endothelial apoptosis, claimed in instant claims 1 and 4. Furthermore, the Jain et al reference does not teach nor suggest the specific regimen recited in claims 3 and 7.

Thus, instant claims 1, 2, 3, 4, 6 and 7 are free of the prior art of record.

Conclusion:

4. Claims 1, 2, 3, 4, 6 and 7 are allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

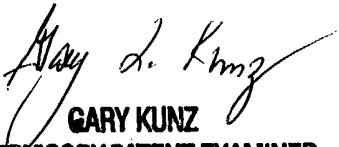
Fozia Hamud
Patent Examiner
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26 March 2004


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SUPERVISORY PATENT EXAMINER
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